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Causes and outcomes of emergency presentation of rectal cancer

HarryComber[1]

Linda Sharp[2]

Marianna de Camargo Cancela[3]

Trutz Haase[4]

Howard Johnson[5]

Jonathan Pratschke[6]

1. National Cancer Registry, Ireland
2. Institute of Health & Society, Newcastle University, United Kingdom
3. Brazilian National Cancer Institute, Division of Population Research, Rio de Janeiro, Brazil
4. Social and Economic Consultant, Dublin, Ireland
5. Health & Wellbeing Directorate Health Intelligence Unit, Health Service Executive, Ireland
6. Department of Economics and Statistics, University of Salerno, Italy

Corresponding author

Dr Harry Comber

Interim Director

National Cancer Registry

Building 6800

Cork Airport Business Park

Kinsale Road

Cork

T12 CDF7

Ireland

Telephone +353214318014

Email: h.comber@ncri.ie

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Novelty and impact statement

We have distinguished various causes and effects of emergency presentation of rectal cancer, using a novel application of structural equation models to survival modelling. Living in an affluent area, private patient status and being married reduced hazard indirectly, by reducing emergency presentation. Emergency presentation was less likely to result in optimal treatment or admission to a high caseload hospital. Patient education and earlier access to endoscopic investigation for public patients could reduce emergency presentation.

Summary

Emergency presentation of rectal cancer carries a relatively poor prognosis, but the roles and interactions of causative factors remain unclear. We describe an innovative statistical approach which distinguishes between direct and indirect effects of a number of contextual, patient and tumour factors on emergency presentation and outcome of rectal cancer.

All patients diagnosed with rectal cancer in Ireland 2004-2008 were included. Registry information, linked to hospital discharge data, provided data on patient demographics, comorbidity and health insurance; population density and deprivation of area of residence; tumour type, site, grade and stage; treatment type and optimality; and emergency presentation and hospital caseload. Data were modelled using a structural equation model with a discrete-time survival outcome, allowing us to estimate direct and mediated effects of the above factors on hazard, and their inter-relationships.

2,750 patients were included in the analysis. 12% had emergency presentations, which increased hazard by 80%. Affluence, private patient status and being married reduced hazard indirectly by reducing emergency presentation. Older patients had more emergency presentations, while married patients, private patients or those living in less deprived areas had fewer than expected. Patients presenting as an emergency were less likely to receive optimal treatment or to have this in a high caseload hospital.

Apart from stage, emergency admission was the strongest determinant of poor survival. The factors contributing to emergency admission in this study are similar to those associated with diagnostic delay. The socio-economic gradient found suggests that patient education and earlier access to endoscopic investigation for public patients could reduce emergency presentation.

Key words: rectal, emergency, survival, deprivation, insurance

Introduction

Rectal cancer commonly presents as an emergency, and in up to 15% of cases the first presentation is unplanned [1]. Patients presenting as an emergency tend to have poorer survival [1–4]. Emergency presentation may have been preceded by bowel obstruction, vomiting, haemorrhage or other co-morbidity, contributing to poorer post-operative survival. However the survival deficit persists for up to one year post-operatively [4], in part due to the more advanced stage of the disease. Patients who present as an emergency are also more likely to be older, poorer, unmarried and to have more co-morbid conditions [2,4] and to present to non-specialist centres.

Most quantitative investigations of the factors leading to emergency presentation and delay in diagnosis have used Cox proportional hazards models, in which the relationship between prognostic factors is dealt with by adjustment, obscuring the role of mediating factors. This approach does not permit measurement of the extent to which any factor exerts a direct influence on the hazard, or an indirect one, mediated by one or more other factors.

Our primary objective was to assess the impact of socio-economic inequalities—in particular age, deprivation, marital status and possession of private health insurance—on survival from rectal cancer, and the role of emergency presentation in the observed variation in outcomes. Inequality in outcome is an important topic in itself, but variations between different groups can shed further light on the overall determinants of survival from rectal cancer.

Methods

All cases of carcinoma of rectal/rectosigmoid cancer (ICD 10 sites C19 and C20) registered by the Irish National Cancer Registry (NCR) as incident during 2004-2008 were included in this study. The Registry has registered all incident cancers in the population of Ireland since 1994; completeness of registration of colon cancers has been estimated to be at least 97-98% [5]. Patients who received no active tumour-directed treatment, defined as any resection, surgery (excluding bypass, reconstructive and cosmetic procedures), chemotherapy or radiotherapy with a primary aim of removing or reducing the tumour in the year following diagnosis, were excluded from analysis.

Information on patient age, sex and marital status, tumour stage, grade and treatment was obtained from NCR data. A Haase Pratschke affluence/deprivation score [6] was assigned to each case, based on the area of residence of the patient at the time of diagnosis. Population density of the area of residence was obtained from the 2006 census of population [7] and divided into approximate population tertiles of <1, 1-14.99 and ≥15 person per ha.

Treatment optimality was determined by comparison with the stage-specific recommendations of the National Comprehensive Cancer Network (NCCN) version 4.2013 [8] and classified as sub-optimal (less intensive treatment, or fewer modalities, than recommended by NCCN guidelines) or optimal/more aggressive (treatment according to the guidelines or using additional modalities).

Hospital of main treatment was determined for each patient from NCR data. In most cases the main hospital was that in which the patient had their major surgical procedure. For patients not having surgery (17%) the main hospital was defined as that of radiotherapy, of chemotherapy or other tumour-directed treatment. Caseload for the main hospital was calculated as the annual average number of rectal cancer patients admitted during the study period, whether or not they received active treatment. Hospitals were classified as “low caseload” if 100 or fewer rectal cancer patients were admitted annually, and as “high caseload” otherwise.

Information on admission type (planned or emergency), co-morbidity and public/private patient status was added by linkage to the hospital in-patient episode (HIPE) database, which was available for all patients admitted to public hospitals. For patients who had no admissions to public hospitals (222, 6.5%), this information was coded as “planned”, the modal value. Co-morbidity was calculated using the Charlson score, excluding the rectal cancer from the calculation. For 462 (15%) of patients no information was available on comorbidity; these were treated as having the modal value of 0. Information on health insurance was inferred from whether or not patients were treated privately. Uninsured patients in Ireland bear the full cost of private care in both public and private hospitals and rarely opt for this, while insured patients normally opt for private care. We therefore assumed that patients treated privately in public hospitals, as indicated in HIPE, and all those treated in private hospitals, had private health insurance.

Survival was calculated by linkage to death certificates provided by the Central Statistics Office, which gave date and cause of death. All patients not confirmed by this linkage to be dead were considered alive on the censoring date of 31/12/2011. Survival was modelled using a discrete-time survival model, which allows a survival outcome to be included within an arbitrarily complex Structural Equation Model [9,10]. The discrete-time survival model is very valuable for the present analysis, as it allows us to treat the influence of patient characteristics as being potentially mediated by emergency admission, caseload, stage of disease and treatment optimality, with treatment also depending on the aforementioned variables. In order to test these mediated effects, it is necessary to estimate a Structural Equation Model with a discrete-time survival outcome, a complex statistical model which can now be estimated using commercially-available software. This novel approach has the potential to shed light on an important and policy-relevant set of research questions regarding pathways of influence and mediation effects.

Figure 1 shows the model structure and all variables available for analysis, which were grouped into background variables—patient characteristics, tumour characteristics, contextual measures and year of diagnosis—and process of care variables—stage of disease, type of admission, treatment optimality and hospital caseload. The model examines the relationship of background characteristics (age, sex, deprivation, marital status, urban/rural residence, tumour site, grade and year of diagnosis) to stage at diagnosis, and the influence of background characteristics, as well as stage of disease, hospital caseload and planned/emergency presentation, on treatment optimality. Caseload, late stage, optimum treatment and planned/emergency presentation were also regressed on background characteristics. The model also allows all of the above variables to influence survival directly.

In order to simplify the calculation and interpretation of the indirect effects, we report results for a model which specifies classical linear regression equations for all dependent variables, regardless of their measurement scale (with the exception of the dichotomous survival indicators). All models were estimated using version 5.21 of the software package MPlus [10] using the MLR estimator.

Results

Patient, cancer and treatment characteristics

Of 3,517 rectal carcinomas incident in 2004-2008, 2,750 (78%) had at least one episode of tumour-directed treatment and were included in the analysis. Of these, 88% of patients had a planned admission, while 12% were admitted as an emergency (Table 1) and 83% had surgery. Emergency admission was significantly more common in older patients and in those who were unmarried, smokers, those with one or more co-morbid conditions, public patients and those living in the most deprived areas or living in rural areas. Proximal cancers more often presented as an emergency, as did those in more advanced stages or with unknown grade. Cancers presenting as an emergency had less aggressive treatment and were more likely to be treated in low caseload hospitals.

Statistical models of hazard: direct effects

At the end of the study period, 29% of emergency admissions were alive, compared to 46% of those admitted routinely In multivariate analyses, considering direct effects only, emergency admission increased the hazard by 80% (HR compared to planned admission 1.80, 95% confidence interval (CI) 1.48, 2.19) (Table 2). Other variables which were independently and directly associated with increased hazard were older age, presence of comorbidity, high-grade tumour and more advanced stage; lower hazard was associated with being married, being a private patient, and having cancer sited in the rectum rather than the rectosigmoid junction.

Statistical models of hazard: indirect effects

Increasing affluence, private patient status and married status indirectly reduced the hazard by reducing the rate of emergency admission (Table 3). Private patient status also reduced the hazard through an indirect effect on stage. No other statistically significant indirect effects were seen, and the only significant combined indirect effect (i.e. considering all potential pathways) involved private patient status.

Statistical models of mediating factors

Table 4 shows the multivariate analysis of factors associated with emergency presentation. Factors associated, in multivariate analyses, with a higher rate of emergency presentation were older age, more advanced stage or higher grade of cancer, cancer site in the rectum and residence in the Western region; those associated with a lower risk were being married, being a private patient, residing in the Southern region and (marginally) residence in a less deprived area. Patients first admitted as an emergency were less likely to receive optimal (or more aggressive) treatment or to have their main treatment in a high caseload hospital.

A higher rate of optimal (or more aggressive) treatment was seen in married patients and those with more advanced disease, while a lower rate was seen in patients living in less deprived areas and those who were admitted as an emergency. Treatment in a high caseload hospital was more frequent in patients from less deprived areas and those with more comorbidity, and less frequent in those living in areas outside the Dublin/Mid-Leinster region or with medium or low population density, and for emergency admissions. Later stage cancers were diagnosed more commonly in patients with high-grade cancers and less frequently amongst older or private patients, or those with one or more comorbid conditions.

Discussion

We have used a relatively novel method, based on the principles of structural equation modelling, which can model direct and indirect effects of prognostic factors on the hazard in a sensitive and time-dependent way. This model is fundamentally different from the classical linear regression model or ANOVA, as it includes structured relationships between variables Our primary objective was to assess the direct and indirect impacts of socio-economic inequalities—in particular age, deprivation, marital status and possession of private health insurance—on survival from rectal cancer, and the role of emergency presentation in the observed variation in outcomes.

In this large population-based study, 12% of first admissions for diagnosis or treatment of rectal cancer were as an emergency. Apart from cancer stage, emergency admission had the strongest direct effect on poor survival, which makes it particularly important to better understand what influences it and how it inter-relates with other factors that may influence survival. In Ireland, although some of the larger private hospitals have emergency rooms, most emergency admissions will be to public hospitals. However patients with private health insurance who present in this way will be recorded as private patients by the public hospital, so we do not consider that having health insurance, or being a private patient, introduces any bias in the designation of patients as public or private.

We succeeded in estimating and testing a number of indirect effects and showed that emergency admission mediates a significant part of the influence of deprivation, private health insurance and marital status on survival. Emergency presentations pose complex clinical challenges [11,12], and are associated with advanced stage and co-morbidity [4,13–15] and a high rate of post-operative complications [14]. Some of the adverse impact of emergency admission may be mitigated by admission to a specialist centre which can deal with these complexities, and there may be a case for transfer to a specialist centre for definitive surgery.

Affluence and health insurance had direct effects on survival, independent of any of the other prognostic factors studied. This may be due to residual confounding [4] due to undetected comorbidity—for instance, the prevalence of smoking and obesity is higher in more deprived populations in Ireland [16]. Although our analysis adjusted for comorbidity, this probably does not capture more subtle levels of general unfitness or lifestyle behaviours that are associated with poor survival. As the patients who were never admitted to public hospitals were assigned a co-morbidity score of 0, co-morbidity was not fully adjusted for in these patients, which would result in a slight under-estimation of the positive effect of health insurance on survival.

Emergency admission of rectal cancer carries a much higher mortality than planned admission regardless of cancer stage at presentation [4,14,17]. It is not possible to estimate directly from our data, how many emergency admissions would be "preventable" but as under 6% of private patients in the most affluent areas had emergency admission compared to 20% of public patients in the most deprived areas, a significant number of emergency admissions seems avoidable. The factors contributing to emergency admission in this study are similar to those associated with diagnostic and treatment delay [1,15,18–20]. Almost all emergency admissions are likely to have been preceded by symptoms, although in a minority of cases the disease may have been occult prior to presentation [21]. Any delay, whether due to patient or health system factors [22–26], will make progression and emergency admission more likely.

Patients may delay acting on symptoms for reasons which are cultural, attitudinal, financial, social or geographical [3,18,27–29]. Delay and emergency admission may be reduced by programmes of education and information on symptoms. Our finding that emergency admission was more frequent in deprived populations and those living alone points to the importance of social support and easy access to health advice.

The commonest causes of health system delay are late or inappropriate referral by general practitioners and delays in access to investigation (e.g. endoscopy). Although median delays are short relative to the natural history of the disease, patients with very long delays are likely to eventually present as emergencies, with a significant impact on survival. General practitioners have been shown, in a number of countries, to delay before referring patients with symptoms of bowel cancer for investigation, despite the risks of obstruction, perforation or haemorrhage [4,13,14,30]. These symptoms (even those which are alarming, such as rectal bleeding) have a low positive predictive value [31–34] and patients with vague or non-specific symptoms may experience long delays, potentially ending in emergency admission. As private patients in Ireland have a lower GP consultation rate than average, a higher level of use of GP care does not seem to have a major effect on diagnostic delay [16]. It has been suggested that the GP's "gatekeeper" role results in fewer and later referrals of patients with suspect symptoms [35,36], and it is reasonable to assume that private health insurance reduces emergency presentation by allowing rapid access by GPs to specialist assessment and endoscopy. Waiting times for endoscopy in Ireland are much shorter for private patients. At the end of 2014, 4850 public patients (37% of those on the waiting list) had been waiting for more than 13 weeks for GI endoscopy [37], while waiting times for private endoscopy, urgent or routine, are of the order of a week [38]. Public patients with non-threatening symptoms are therefore at higher risk of emergency admission than private patients, who can opt to bypass queues for secondary care [39]. However, although emergency admission would be less frequent if doctors referred earlier and more often [20] investigation of suspected colorectal cancer is expensive [40] and there must be a balance between over-and under-referral. The consequence of more open access may be fewer emergency admissions but higher costs for investigation of the many symptomatic patients who turn out not to have cancer [41].

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Table 1. Patient, cancer and treatment characteristics by admission type

	planned (N=2708)		emergency (N=342)		Total	chisquare
year of incidence						
2004	453	(86%)	73	(14%)	526	0.146
2005	459	(86%)	72	(14%)	531	
2006	453	(86%)	74	(14%)	527	
2007	537	(90%)	61	(10%)	598	
2008	506	(89%)	62	(11%)	568	
vital status at end of followup						
alive	1304	(93%)	100	(7%)	1404	0.001
dead	1104	(82%)	242	(18%)	1346	
age at diagnosis						
<60	702	(92%)	63	(8%)	765	<0.001
60-69	697	(89%)	86	(11%)	783	
70-79	703	(86%)	112	(14%)	815	
80+	306	(79%)	81	(21%)	387	
sex						
male	1,578	(88%)	210	(12%)	1,788	0.134
female	830	(86%)	132	(14%)	962	
marital status						
married	1,536	(90%)	173	(10%)	1,709	<0.001
unmarried	872	(84%)	169	(16%)	1,041	
smoking status						
current smoker	433	(83%)	89	(17%)	522	<0.001
never smoked	933	(86%)	149	(14%)	1,082	
ex-smoker	536	(91%)	55	(9%)	591	
unknown	506	(91%)	49	(9%)	555	
payment status						
private patient	876	(93%)	66	(7%)	942	<0.001
public patient	1,447	(84%)	269	(16%)	1,716	
unknown	85	(92%)	7	(8%)	92	
area deprivation quintile						
1 (least deprived)	463	(90%)	52	(10%)	515	<0.001
2	504	(89%)	65	(11%)	569	
3	496	(90%)	57	(10%)	553	
4	475	(88%)	62	(12%)	537	
5 (most deprived)	465	(82%)	103	(18%)	568	
region of residence						
Dublin/Mid-Leinster	644	(88%)	84	(12%)	728	<0.001
Dublin/North-east	457	(89%)	59	(11%)	516	
South	739	(91%)	71	(9%)	810	
West	558	82%)	126	(18%)	684	
urban/rural residence						
high-urban	843	(89%)	106	(11%)	949	0.007
intermediate-urban	532	(90%)	59	(10%)	591	
rural	825	(85%)	144	(15%)	969	
cancer site						
rectosigmoid	528	(84%)	103	(16%)	631	0.001
rectum	1,880	(89%)	239	(11%)	2,119	
stage at diagnosis						
Stage I	390	(94%)	25	(6%)	415	<0.001
Stage II	589	(85%)	100	(15%)	689	
Stage III	953	(89%)	115	(11%)	1,068	
Stage IV	467	(82%)	100	(18%)	567	

unknown	9	(82%)	2	(18%)	11	
grade						
low/intermediate	1,872	(89%)	238	(11%)	2,110	0.002
high	249	(86%)	42	(14%)	291	
unknown	287	(82%)	62	(18%)	349	
Charlson comorbidity score						
0	1,666	(88%)	229	(12%)	1,895	0.001
1	297	(82%)	66	(18%)	363	
2	170	(81%)	39	(19%)	209	
unknown	275	(97%)	8	(3%)	283	
treatment intensity						
less aggressive	968	(84%)	182	(16%)	1,150	<0.001
optimal	1,259	(89%)	153	(11%)	1,412	
more aggressive	181	(96%)	7	(4%)	188	
caseload of main hospital						
1 (lowest caseload quintile)	534	88%)	70	(12%)	604	<0.001
2	434	84%)	85	(16%)	519	
3	445	83%)	88	(17%)	533	
4	461	93%)	35	(7%)	496	
5 (highest caseload quintile)	499	93%)	39	(7%)	538	
unknown	35	58%)	25	(42%)	60	

Table 2. Direct effects of patient, cancer and treatment characteristics on hazard ratio

Variable	***Value***	**Hazard ratio (95% confidence intervals)**
emergency admission		
	no	1.00
	yes	**1.80 (1.48, 2.19)**
sex		
	female	1.00
	male	1.26 (0.53, 2.98)
age		
	per 10 year increase	**1.38 (1.25, 1.52)**
age and sex interaction		
	other	1.00
	male aged 70+	0.98 (0.85, 1.12)
deprivation score		
	per unit score	0.67 (0.39, 1.16)
marital status		
	never married	1.00
	married	**0.85 (0.74, 0.98)**
private patient		
	no	1.00
	yes	**0.72 (0.61, 0.84)**
HSE area		
	Dublin Mid-Leinster	1.00
	Dublin North-east	1.09 (0.88, 1.36)
	South	1.05 (0.88, 1.25)
	West	1.05 (0.86, 1.28)
urban/rural residence		
	high	1.00
	medium	1.14 (0.95, 1.36)
	low	1.00 (0.84, 1.19)
	unknown	1.03 (0.80, 1.33)
tumour grade		
	low/intermediate	1.00
	high	**1.77 (1.45, 2.15)**
stage		
	I/II	1.00
	III/IV	**2.86 (2.59, 3.15)**
comorbidities		
	no	1.00
	yes	**1.42 (1.21, 1.66)**
optimal treatment regime		
	no	1.00
	yes	0.90 (0.77, 1.06)
hospital caseload		
	0-200 cases/year	1.00
	>200 cases/year	0.90 (0.78, 1.03)
site		
	rectosigmoid	1.00
	rectum	**0.84 (0.72, 0.99)**
year of diagnosis		**0.92 (0.89, 0.96)**

Note: Values in bold denote statistically significant values

Table 3. Indirect effects of affluence, private patient status and marital status on hazard, mediated through cancer and treatment characteristics; coefficients and 95% confidence intervals

	Effect of		
Mediated through:	**affluence**	**private patient**	**never married**
optimal treatment	0.02 (-0.02, 0.06)	0.00 (0.00, 0.01)	-0.01 (-0.01, 0.00)
high caseload hospital	-0.04 (-0.10, 0.01)	**0.00 (-0.01, 0.00)**	0.00 (0.00, 0.00)
late stage	-0.02 (-0.32, 0.28)	**-0.14 (-0.22, -0.05)**	0.03 (-0.05, 0.11)
emergency admission	**-0.07 (-0.14, -0.01)**	**-0.04 (-0.05, -0.02)**	**-0.02 (-0.04, 0.00)**
caseload → treatment	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage → optimal treatment	0.00 (-0.03, 0.03)	0.01 (-0.01, 0.04)	0.00 (-0.01, 0.01)
late stage → high caseload hospital	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage→ emergency admission	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
emergency admission optimal treatment	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
emergency admission→ high caseload hospital	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage → high caseload hospital → optimal treatment	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage →emergency admission→ optimal treatment	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage →emergency admission→ high caseload hospital	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
late stage →emergency admission →high caseload hospital → optimal treatment	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
All indirect effects	-0.12 (-0.41, 0.18)	**-0.16 (-0.25, -0.08)**	0.00 (-0.08, 0.08)
Direct effect	-0.40 (-0.94, 0.15)	**-0.33 (-0.48, -0.17)**	**-0.16 (-0.30, -0.02**)
Total effect	-0.51 (-1.11, 0.08)	**-0.49 (-0.66, -0.32)**	-0.16 (-0.31, 0.00)

Note: Values in bold denote statistically significant values

Table 4. Regression coefficients (95% confidence intervals) of optimum treatment, caseload, tumour stage and first hospital admission type on explanatory variables

variable	values	emergency admission	optimum or more aggressive treatment	main treatment in high caseload hospital	late stage
year of diagnosis (per year)		-0.01 (-0.01, -0.01)	0.00 (-0.02, 0.02)		0.00 (-0.02, 0.02)
sex	**female**				
	male	-0.01 (-0.15, 0.13)	-0.04 (-0.24, 0.16)	0.03 (-0.17, 0.23)	0.27 (-0.14, 0.68)
age	**per 10 year increase**	0.02 (0.00, 0.04)	**-0.10 (-0.12, -0.08)**	-0.02 (-0.04, 0.00)	-0.05 (-0.09, -0.01)
age and sex	**other**	0.00	0.00	0.00	0.00
	male aged 70+	0.00 (-0.02, 0.02)	0.01 (-0.03, 0.05)	0.00 (-0.04, 0.04)	-0.03 (-0.09, 0.03)
deprivation score	**per unit score**	-0.12 (-0.24, 0.00)	**-0.21 (-0.35, -0.07)**	**0.40 (0.26, 0.54)**	-0.02 (-0.31, 0.27)
marital status	**never married**	0.00	0.00	0.00	0.00
	married	-0.04 (-0.06, -0.02)	**0.05 (0.01, 0.09)**	-0.01 (-0.05, 0.03)	0.03 (-0.05, 0.11)
private patient	**no**	0.00	0.00	0.00	0.00
	yes	-0.06 (-0.08, -0.04)	-0.03 (-0.07, 0.01)	0.02 (-0.02, 0.06)	-0.13 (-0.21, -0.05)
HSE area	**Dublin Mid-Leinster**	0.00	0.00	0.00	0.00
	Dublin North-east	-0.01 (-0.05, 0.03)	0.01 (-0.05, 0.07)	**-0.14 (-0.20, -0.08)**	-0.11 (-0.23, 0.01)
	South	-0.04 (-0.08, 0.00)	-0.05 (-0.11, 0.01)	**-0.13 (-0.19, -0.07)**	0.04 (-0.06, 0.14)
	West	0.05 (0.01, 0.09)	0.01 (-0.05, 0.07)	**-0.22 (-0.28, -0.16)**	0.09 (-0.03, 0.21)
urban/rural residence	**high (urban)**	0.00	0.00	0.00	0.00
	medium	-0.01 (-0.05, 0.03)	0.01 (-0.05, 0.07)	**-0.23 (-0.29, -0.17)**	0.02 (-0.08, 0.12)
	low (rural)	0.02 (-0.02, 0.06)	0.02 (-0.04, 0.08)	**-0.31 (-0.35, -0.27)**	-0.04 (-0.14, 0.06)
	unknown	0.02 (-0.02, 0.06)	0.02 (-0.06, 0.10)	**-0.29 (-0.37, -0.21)**	0.00 (-0.14, 0.14)
site	**rectosigmoid**	0.00	0.00	0.00	0.00
	rectum	0.05 (0.01, 0.09)	**-0.22 (-0.26, -0.18)**	-0.10 (-0.14, -0.06)	0.06 (-0.02, 0.14)
tumour grade	**low/intermediate**	0.00	0.00	0.00	0.00
	high	0.02 (-0.02, 0.06)	-0.01 (-0.07, 0.05)	**0.03 (-0.03, 0.09)**	0.47 (0.37, 0.57)
stage	**I/II**	0.00	0.00	0.00	
	III/IV	0.03 (0.01, 0.05)	**0.03 (0.01, 0.05)**	0.01 (-0.01, 0.03)	
comorbidities	**no**	0.00	0.00	0.00	0.00
	yes	0.06 (0.02, 0.10)	0.01 (-0.03, 0.05)	**0.06 (0.02, 0.10)**	-0.10 (-0.20, 0.00)
first admission	**booked**		0.00	0.00	
	emergency		**-0.09 (-0.15, -0.03)**	-0.03 (-0.09, 0.03)	
hospital caseload	**0-100 cases/year**		0.00		
	>100 cases/year		0.02 (-0.02, 0.06)		

Note: Values in bold denote statistically significant values